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EXAMINER

NAFF, DAVID M

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 12/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/611,674

Applicant(s)

BRAITHWAITE ET AL.

Examiner

David M. Naff

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-90 is/are pending in the application.
- 4a) Of the above claim(s) 81-90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/24/05, 6/14/04</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims in the application are 1-90.

Election/Restrictions

Restriction to one of the following inventions is required under

5 35 U.S.C. 121:

I. Claims 1-80, drawn to a method of attachment of cells to a template, classified in class 435, subclass 174.

II. Claims 81-86, drawn to an article, classified in class 428, subclass 411.1+.

10 III. Claims 87-90, drawn to a method of coating with a polymer, classified in class 427, subclass 384.

The inventions are distinct, each from the other because:

Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together
15 and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions involve in one case (I) cells in culture and in the other case (III) nonliving polymers.

Inventions I and II are related as process of making and product
20 made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the article as claimed can be made

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by a materially different process such as making cell layers apart from templates.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II or
5 III, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

10 During a telephone conversation with John Isacson Jr on July 11, 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-80. Affirmation of this election must be made by applicant in replying to this Office action. Claims 81-90 are withdrawn from further consideration by the examiner, 37
15 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the
20 application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims examined on the merits are 1-80.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C.

112:

5 The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10 Claims 1-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15 Claim 1 is confusing and unclear by requiring producing a templated extracellular matrix in the preamble and not requiring a final step that will result in production of the matrix. Merely contacting cells with the template as in the last step of the claim will not produce the matrix. After contacting, the cells will have to be cultured to produce the matrix, and a step of culturing to produce the matrix should be recited.

20 In the last line of claim 1, "cells activated for producing a templated extracellular matrix" is uncertain as to meaning and scope since the change in the cells when activated is uncertain. How one would know when the cells are activated and not activated is uncertain.

25 In line 2 of claim 2, "texture surface" is uncertain as to meaning. Should this be "textured surface"?

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In claim 3, "aligned polymer etched silicon" is unclear as to material aligned, and the material on which it is aligned. If the polymer has been aligned on the etched silicon, how would one know when the polymer is aligned and not aligned?

5 Claim 4 is unclear by requiring a use without setting forth method steps of performing the use. Additionally, in line 2 of the claim "and other structured connective tissue" is unclear as to tissue required. Being a structured connective tissue is relative and subjective.

10 In line 2 of claim 4 and line 1 of claim 6 and where recited in other claims "such as" makes the claims uncertain as to claim metes and bounds. It is uncertain as to whether a condition, step and/or material claimed as "such as" is to be patentably limiting. Putting in the claims limitations that are not patentably limiting, beclouds
15 limitations that are intended to be patentably limiting.

 Claim 5 is unclear as to the relationship of the steps required in lines 5-9 to the previous steps required in lines 2-4. The claim requires no functional relationship between the steps of lines 2-4 and the steps of lines 5-9.

20 Claim 5 is unclear in line 3 as to what is subjected to shear flow, and physical phenomena that results in shear. Without knowing what is subjected to shear flow and the cause of shear flow, one cannot determine when shear flow exists and does not exist. In line 3, the meaning of "polymer structures" is uncertain since a step that
25 produces a polymer structure has not been required. Additionally, it

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is uncertain how one would know when a polymer structure is aligned and not aligned since a structure capable of alignment has not been required and the claim fails to specify a direction of alignment.

Line 4 of the claim is unclear by requiring controlling

5 polymerization, and not requiring a step of "polymerization".

Polymerization does not have antecedent basis. In line 5, the claim is unclear as to the relationship of generating a first layer to the previous forming of an alignment of polymer structures.

Claim 7 is unclear as to precisely where in claim 6 the steps of
10 claim 7 are performed. Is the substrate in line 4 of claim 7 the substrate of claim 6, or some other substrate. The "shearing flow" required in line 5 is unclear for the type of reasons set forth above in regard to shear flow. In line 6 of the claim, there is not clear antecedent basis for "the self-assembling collagen fibrils". A step
15 of preparing the fibrils has not been previously set forth, and the relationship of orientation of fibrils to the previous step is unclear. In line 8, "generating successive layers" is confusing since a step that produces the layers has not been set forth. It is uncertain as to what the layers are made of, and the relationship of
20 generating the layers to the previous step. Bridging lines 8 and 9, there is no antecedent basis for "the component". A previous step of forming a component is not required.

In line 2 of claim 8, the range is uncertain by not requiring a definite lower limit. How far does "sub-micron" extend below "micron"
25 as a lower limit of the range?

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Claim 11 is confusing by requiring an angle range of between 0 to 180 degrees. If this range encompasses 0 degrees, 0 degrees is not an angle.

5 Claim 13 is unclear as to a rate of spinning that is "50 to 50,000 Hz" since spinning is normally expressed as revolutions per time period. The property of spinning that is "Hz" is uncertain, and it is uncertain how one would know when spinning is within and not within the range.

10 In line 1 of claim 15, there is not antecedent basis in claim 5 for "the atmosphere".

In line 2 of claim 16, there is not antecedent basis in claim 5 for "the polymerization kinetics and morphology". Additionally, it is uncertain as to physical phenomena that constitutes "polymerization kinetics" and "polymerization morphology", and how one would know when
15 solution conditions are modulated to control polymerization kinetics and morphology.

Claim 17 is unclear in line 2 as whether the polymer predominantly aligned is the polymer chains or some other polymer structure that is aligned.

20 Claim 18 is unclear as to physical phenomena that constitutes "angular rotation" (line 1), and that constitutes "confinement to orient the polymerized polymers". Additionally, there is not antecedent basis for "the polymerized polymers". Claim 5 does not require polymerizing polymers.

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Claims 19 and 20 are confusing by not having clear antecedent basis for "input flow rate", "solution viscosity" and "substrate rotational velocity". Where in claims 5 and 18 on which claim 19 depends, is there input flow rate, solution viscosity and substrate rotational velocity?

Claim 21 is confusing by not having clear antecedent basis in claim 5 for aligned polymer layers. A step of preparing aligned polymer layers is not required in claim 5.

There is not clear antecedent basis in claim 5 for "construct of a plurality of aligned layers" in line 1 of claim 22. Claim 5 does not require producing a construct of a plurality of aligned layers.

In claim 23, there is not clear antecedent basis in claims 5 and 7 for "the alignment of the polymers in a plane of second and subsequent layers", and in claims 24 and 25 for "the alignment of the polymers in a plane of a layer in a second and subsequent layers". A step of preparing this alignment of polymers and preparing second and subsequent layers has not been previously required. Additionally, there is not clear antecedent basis for "alignment of the polymers in a plane of the first layer" as required in the last line of claim 23-25. Bridging lines 2 and 3 of claim 25, physical phenomena that is an angular relationship is uncertain.

Claim 26 does not have antecedent basis for "the monomer" since claim 5 does not require a monomer.

Claims 27 and 28 are unclear by requiring collagen to be a monomer since claim 6 requires collagen as a polymer. How can

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collagen be both a monomer and polymer? Claim 28 is further unclear as to how "extracted" defines the collagen used. The difference in an extracted and non-extracted collagen is uncertain.

5 In claim 29, there is not antecedent basis for "the polymerizing solution". This solution has not been previously required in a claim on which claim 29 depends.

Claims 31-33 and 51 are confusing by reciting "injected" since claim 5 requires "controlling flow of a polymer solution" rather than the polymer solution being injected. Additionally, in line 1 of claim 10 33, there is not antecedent basis for "the material".

In line 1 of claim 33 and where recited in other claims "preferably" makes the claims uncertain as to metes and bounds for the same type of reason set forth above in regard to "such as".

Claim 34 is unclear as to where in the method of claim 5 the 15 "post-processing step" is carried out. Where in claim 5 is effluent produced and what is the material in claim 5 that is an effluent? Additionally, it is uncertain in line 2 of claim 34 as to physical phenomena that is "spinning off any effluent material from the substrate".

20 Claim 35 is unclear by reciting "comprising the substrate" in line 1 since claim 5 already requires a substrate. Claim 35 is further unclear as to whether the "substrate holder" is different from the "device having a substrate" in claim 5. If the holder and device are not the same, where is the holder present in claim 5 relative to 25 the device? Claim 35 is further unclear as to what will constitute

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the holder being modified to minimize waste of polymerization solution as required in line 2. Also, there is no antecedent basis in claim 5 for "polymerization solution".

5 In line 2 of claim 36, it is uncertain as to the relationship of "(3 mg/ml)" to the collagen type I. If 3 mg/ml is the amount of collagen present, the claims should recite "3 mg/ml of collagen type I" in place of "collagen type I (3 mg/ml)".

In line 1 of claims 37 and 38, there is not clear antecedent basis for "the viscosity".

10 Claim 41 is unclear how surface roughness is defined by being less than 10 microns. What structural part of the surface is less than 10 microns?

Claim 43 is unclear by requiring substrate treatment that controls adhesion of the polymer and wetting of the solution and not
15 having clear antecedent basis for polymer adhesion to the substrate and solution wetting of the substrate. Furthermore, the claim is unclear as to the relationship of the polymer and solution to the substrate, i.e. is the polymer adhering to the substrate and is the solution wetting the substrate?

20 Claim 44 is uncertain as to material that is "micro90(Brand) cleaner". This appears to be a tradename, and its composition and how it is produced is unknown. If the product having this tradename cannot be obtained commercially, it will be uncertain as to when the product is being used.

Claim 49 is confusing how claim 5 is further limited by requiring a substrate pattern that will constrain flow since claim 49 does not specify the flow in claim 5 that the substrate pattern constrains. Furthermore, it is unclear as to whether the substrate of claim 49 is
5 that of claim 5 or some other substrate.

Claim 50 is confusing by not having clear antecedent basis in claim 5 for "surface of the substrate" and "atmospheric conditions". Also, the claim is unclear as to material in claim 5 is undergoing "self-assembly".

10 In line 2 of claim 51, there is not clear antecedent basis in claim 5 for "the polymerization process and final morphology of the layer". Additionally, in line 1 of the claim, it is uncertain as to whether "additives" is requiring a plurality of additives added together. This also applies to "proteoglycans" in claim 52. It is
15 suggested that claim 51 recite "an additive is" in place of "additives are", and claim 52 recite "additive is proteoglycan" in place of "additives are proteoglycans".

Claim 53 is unclear by requiring additives to be selected from "at least one of". One additive cannot be a plurality of additives
20 required by "additives". In line 1, "additives are" should be changed to "additive is". This also applies to "proteoglycans are" in claims 54 and 79.

Claim 54 does not have antecedent basis for "the proteoglycans", and claim 55 does not have antecedent basis for "the percent (by
25 weight) of added proteoglycans". Claim 51 does not require

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proteoglycans. It is suggested claims 54 and 55 be dependent on claim 52.

In line 1 of claims 55, 56 and 80, and line 2 of claim 77, "proteoglycans" should be "proteoglycan" to be consistent with the
5 change suggested above.

Claim 57 is unclear by reciting "maintaining-----in culture" since a culture has not been established. It is suggested that the claim instead recite "culturing the first population of cells contained by the nanostructured artificial template".

10 Claim 58 is confusing and unclear by requiring a further step in claim 57 of stacking a plurality of templated extracellular matrix layers, and not having antecedent basis in claim 57 for a plurality of templated extracellular matrix layers being produced. Claim 57 does not require producing plurality of the layers, but rather requires
15 producing a templated extracellular matrix. Claim 57 should require producing a templated extracellular matrix layer, and claim 58 should require the method of claim 57 to produce a plurality of the layers, and then require stacking the layers as claimed in claim 58.

Claim 59 does not have antecedent basis in claim 58 for "the
20 multilaminar templated extracellular matrix layer". Claim 58 should be amended in line 3 by inserting --- layer --- after "matrix".

Claim 66 is unclear as to whether the acid, salts and esters are all required together for treatment, or are being used separately.

Claim 67 is unclear as to physical steps required by "made
25 quiescent by the remote of ascorbate". It is uncertain as to the

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state of the fibroblasts when quiescent, and physical phenomena that constitutes "remote of ascorbate".

Claims 70, 72 and 74 are unclear as to the meaning and scope of "unstressed". Being unstressed is relative and subjective.

5 Claim 79 does not have antecedent basis for "the proteoglycans", and claim 80 does not have antecedent basis for "the percent (by weight) of proteoglycans". Claim 76 does not require proteoglycans. It is suggested claims 79 and 80 be dependent on claim 77.

Claim Rejections - 35 USC § 103

10 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

15 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation
25 under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-4, 57, 62, 63, 70, 71 and 76-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton et al (5,962,325) in view of Bessea et al (AV on form 1449).

5 The claims are drawn to producing a templated extracellular matrix by providing a nanostructured artificial template, and contacting the template with cells activated for producing a templated extracellular matrix.

10 Naughton et al disclose culturing stromal cells on a three-dimensional matrix (paragraph bridging cols 10 and 11) to from stromal tissue. During culturing, extracellular matrix protein including collagen is produced in the matrix (col 6, lines 10-21). The three-dimensional matrix can be coated with collagen (col 11, line 12). Cells cultured on the matrix can be chondrocytes, fibroblasts and/or cells capable or producing collagen type II and other collagen types, 15 and proteoglycans which are typically produced in cartilaginous tissues (col 6, lines 15-20, and col 14, lines 20-50).

Bessea et al disclose producing ordered collagen matrices for three-dimensional cell culture. The ordered collagen matrices contain fibrillar organization close to that *in vivo*.

20 It would have been obvious to use as the three-dimensional matrix of Naughton et al, the ordered three-dimensional collagen matrix of Bessea et al to obtain property of the collagen matrix having a fibrillar organization close to that *in vivo*. The collagen matrix is inherently a nanostructured artificial template. After seeding and 25 culturing stromal cells on the matrix as disclosed by Naughton et al,

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the matrix will be a templated extracellular matrix since extracellular matrix protein is produced by the stromal cells during culture as disclosed by Naughton et al (col 6, lines 12-22). The matrix will inherently have a first and second surface as required by claim 58. Adding a growth factor as disclosed by Naughton et al (col 11, lines 39-42) will activate the cells as required by the last line of claim 1. The template being unstressed as in claim 70 and being subjected to tensile stress as in claim 71 would have inherently resulted when using a matrix for stromal cell culture as set forth above. For example, handling the matrix will result in tensile stress, and the matrix will be unstressed during culturing.

Claim Rejections - 35 USC § 103

Claims 58-61, 64, 65, 68, 69 and 72-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-4, 57, 62, 63, 70, 71 and 76-80 above, and further in view of Vacanti et al (6,455,311 B1).

Claim 58 and claims dependent thereon require stacking a plurality of templated extracellular matrix layers to form a multilaminar templated extracellular matrix.

Vacanti et al disclose a laminar structure having multiple layers of tissue. The laminar structure is prepared by forming a mold or template, seeding and culturing cells on the mold or template to produce a tissue layer, removing the tissue layer, and assembling multiple tissue layers to obtain the laminar structure (col 5, lines

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5-25, col 5, lines 25-43, paragraph bridging cols 12 and 13, and col 13, lines 15-30).

When producing stromal tissue on a matrix as disclosed by Naughton et al and using a collagen matrix as suggested by Bessea et al as set forth above, it would have been obvious to produce a laminar structure having multiple layers of tissue as suggested by Vacanti et al. Producing different layers having different cells as in claims 60 and 61 would have been suggested by Vacanti et al producing different tissue layers using different cells (paragraph bridging cols 12 and 13), and Naughton et al using a mixture of cells (col 14, lines 18-20). The template being unstressed as in claim 72, the matrix being subjected to tensile stress as in claim 73, and the matrix being unstressed as in claim 74 would have inherently resulted when producing and using a laminar structure as set forth above.

Claim Rejections - 35 USC § 103

Claims 66 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-4, 57, 62, 63, 70, 71 and 76-80 above, and further in view of Lyons et al (AT3 on form 1449) or Nusgens et al (AX3).

The claims require activating mammalian fibroblasts by treatment with ascorbic acid, or ascorbate salts or esters.

Lyons et al disclose that adding ascorbate to culture medium for primary avian tendon cells stimulates procollagen gene transcription.

Nusgens et al disclose that in fibroblast cultures, vitamin C (ascorbic acid) stimulates collagen production.

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When culturing fibroblasts as the cells of Naughton et al and using a matrix as suggested by Bessea et al as set forth above, it would have been obvious to add ascorbate or ascorbic acid when culturing to stimulate collagen production as suggested by Lyons et al or Nusgens et al.

Claim Rejections - 35 USC § 103

Claims 5-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-4, 57, 62, 63, 70, 71 and 76-80 above, and further in view of Ruberti et al (AS5).

10 Claim 5 and claims dependent thereon require controlling flow of a polymer solution into a device having a substrate and the device generating shear flow to induce alignment of polymer structures to produce the nanostructured artificial template.

15 Ruberti et al disclose nanoscale engineering of type I collagen fibrils to mimic the multiple layers of aligned lamellae in cornea by polymerizing type I collagen on the surface of a rotating substrate under shear conditions to obtain aligned collagen fibrils.

20 When using a collagen matrix as suggested by Bessea et al as the matrix of Naughton et al as set forth above, it would have been obvious to produce the collagen matrix as taught by Ruberti et al to obtain aligned collagen fibrils. The conditions of claims depending on claim 5 would have been obvious from conditions disclosed by the references.

25 Parent application 10/306,825 does not antedate Ruberti et al since the present application is a continuation-in-part of the parent

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application, and the present invention is not disclosed in the parent application. Ruberti et al appears to have been published in 2003 prior to filing of the instant application, and the inventive entity of the present invention is different from the authorship of Ruberti et al since Melotti is an author and not an inventor. Therefore, Ruberti et al is a reference even through inventors Ruberti and Braithwaite are also authors.

Claim Rejections - 35 USC § 103

Claims 5-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-4, 57, 62, 63, 70, 71 and 76-80 above, and further in view of Lee et al (WO 00/34442) (AN) and Agarwal et al (AS).

The claimed invention is described above.

Lee et al disclose applying shear flow stress to smooth muscle cells such that the cells align perpendicular to the direction of flow to produce implantable structures.

Agarwal et al disclose using shear flow to induce orientation during polymerization of rigid rod-like molecules.

When using a collagen matrix as suggested by Bessea et al as the matrix of Naughton et al as set forth above, it would have been obvious to produce the collagen matrix using shear flow to align collagen fibrils as suggested by Lee et al using shear flow to align cells and Agarwal et al using shear flow to align rigid rod-like molecules during polymerization. Since shear flow can align both the cells and the molecules, it would have been expected that shear flow

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will also align collagen fibrils which is desirable due to the fibrils being aligned *in vivo*. The conditions of dependent claims would have been obvious from conditions suggested by the references.

Conclusion

5 Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful,
10 the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR)
15 system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private
20 PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner
Art Unit 1651